

I CLAIM:

1. A method of making an assessment of the likelihood that a human patient who is asymptomatic for coronary artery disease has the disease, the method comprising the steps:

(a) obtaining the level of an atherogenic protein in a sample from the patient,
5 obtaining the level of an acute phase reactant in a sample from the patient, and optionally obtaining the level of an anti-atherogenic protein in a sample from the patient;

(b) obtaining at least one of:

(i) a first cut-point related to the atherogenic protein and a second cut-point related to the acute phase reactant,

10 (ii) a third cut-point related to the atherogenic protein and the acute phase reactant,

(iii) a fourth cut-point related to the atherogenic protein and the acute phase reactant and a fifth cut-point related to the anti-atherogenic protein,

(iv) a sixth cut-point related to the atherogenic protein and a seventh cut-point
15 related to the acute phase reactant and the anti-atherogenic protein,

(v) an eighth cut-point related to the atherogenic protein and the anti-atherogenic protein and a ninth cut-point related to the acute phase reactant,

(vi) a tenth cut-point related to the atherogenic protein, the acute phase reactant, and the anti-atherogenic protein,

20 (vii) an eleventh cut-point related to the atherogenic protein, a twelfth cut-point related to the acute phase reactant, and a thirteenth cut-point related to the anti-atherogenic protein; and

(c) assessing whether the patient is likely to have asymptomatic coronary artery disease based on at least one of the following:

25 (i) a comparison to the first cut-point of a first value related to the level of the atherogenic protein and a comparison to the second cut-point of a second value related to the level of the acute phase reactant,

(ii) a comparison to the third cut-point of a third value related to the levels of the atherogenic protein and acute phase reactant,

(iii) a comparison to the fourth cut-point of a fourth value related to the levels of the atherogenic protein and acute phase reactant and a comparison to the fifth cut-point of a fifth value related to the level of the anti-atherogenic protein,

(iv) a comparison to the sixth cut-point of a sixth value related to the level of the atherogenic protein and a comparison to the seventh cut-point of a seventh value related to the levels of the acute phase reactant and anti-atherogenic protein,

(v) a comparison to the eighth cut-point of an eighth value related to the levels of the atherogenic protein and anti-atherogenic protein and a comparison to the ninth cut-point of a ninth value related to the level of the acute phase reactant,

(vi) a comparison to the tenth cut-point of a tenth value related to the levels of the atherogenic protein, acute phase reactant, and anti-atherogenic protein, and

(vii) a comparison to the eleventh cut-point of an eleventh value related to the level of the atherogenic protein, a comparison to the twelfth cut-point of a twelfth value related to the level of the acute phase reactant, and a comparison to the thirteenth cut-point of a thirteenth value related to the level of the anti-atherogenic protein.

2. The method of claim 1 wherein the atherogenic protein comprises OxLDL (oxidized low density lipoprotein).

3. The method of claim 2 wherein the OxLDL contains at least 60 substituted lysine residues per apo B-100 (apolipoprotein B-100) moiety.

4. The method of claim 1 wherein the acute phase reactant comprises a positive acute phase reactant or a negative acute phase reactant.

5. The method of claim 4 wherein the positive acute phase reactant is selected from the group consisting of C-reactive protein, serum amyloid A, von Willebrand factor, ferritin, and fibrinogen and the negative acute phase reactant is selected from the group consisting of albumin, apo A-I (apolipoprotein A-I), apo A-II (apolipoprotein A-II), and HDL (high density lipoprotein).

6. The method of claim 1 wherein the anti-atherogenic protein comprises HDL.

7. The method of claim 1 wherein the atherogenic protein comprises OxLDL and the acute phase reactant is selected from the group consisting of C-reactive protein and fibrinogen.

8. The method of claim 7 wherein the anti-atherogenic protein comprises HDL.

9. The method of claim 1 wherein step (a) uses an immunological assay to obtain the level of atherogenic protein.
10. The method of claim 9 wherein the immunological assay uses one or more monoclonal antibodies each having an affinity for the atherogenic protein of at least about $5 \times 10^8 \text{ M}^{-1}$.
- 5 11. The method of claim 10 wherein the immunological assay uses at least one of the following monoclonal antibodies to obtain the level of atherogenic protein: mAb-4E6 produced by hybridoma Hyb4E6 deposited with the BCCM (Belgian Coordinated Collections of Microorganisms) under deposit accession number LMBP 1660 CB, mAb-1H11 produced by hybridoma Hyb1H11 deposited with the BCCM under deposit accession number LMBP 1659
10 CB, and mAb-8A2 produced by hybridoma Hyb8A2 deposited with the BCCM under deposit accession number LMBP 1661 CB.
12. The method of claim 1 wherein the atherogenic protein comprises an atherogenic low density lipoprotein and step (a) is conducted using an immunological assay.
13. The method of claim 1 wherein the atherogenic protein comprises OxLDL and an
15 immunological assay is used to obtain the level of atherogenic protein.
14. The method of claim 13 wherein the immunological assay uses one or more monoclonal antibodies each having an affinity for the atherogenic protein of at least about $5 \times 10^8 \text{ M}^{-1}$.
15. The method of claim 13 wherein in step (a) the level of anti-atherogenic protein is obtained and the anti-atherogenic protein comprises HDL.
- 20 16. The method of claim 13 wherein the acute phase reactant is selected from the group consisting of C-reactive protein and fibrinogen.
17. The method of claim 16 wherein in step (a) the level of anti-atherogenic protein is obtained and the anti-atherogenic protein comprises HDL.
18. The method of claim 13 wherein the OxLDL contains at least 60 substituted lysine
25 residues per apo B-100 moiety.
19. The method of claim 18 wherein in step (a) the level of anti-atherogenic protein is obtained and the anti-atherogenic protein comprises HDL.
20. The method of claim 19 wherein the acute phase reactant is selected from the group consisting of C-reactive protein and fibrinogen.

21. The method of claim 12 wherein the immunological assay uses at least one of the following monoclonal antibodies to obtain the level of atherogenic protein: mAb-4E6 produced by hybridoma Hyb4E6 deposited with the BCCM under deposit accession number LMBP 1660 CB, mAb-1H11 produced by hybridoma Hyb1H11 deposited with the BCCM under deposit
5 accession number LMBP 1659 CB, and mAb-8A2 produced by hybridoma Hyb8A2 deposited with the BCCM under deposit accession number LMBP 1661 CB.

22. A method of facilitating the assessment by a medical professional of the likelihood that a human patient who is asymptomatic for coronary artery disease has the disease, the method comprising the steps:

10 (a) obtaining the level of an atherogenic protein in a sample from the patient, obtaining the level of an acute phase reactant in a sample from the patient, and optionally obtaining the level of an anti-atherogenic protein in a sample from the patient;

(b) obtaining at least one of:

15 (i) a first cut-point related to the atherogenic protein and a second cut-point related to the acute phase reactant,

(ii) a third cut-point related to the atherogenic protein and the acute phase reactant,

(iii) a fourth cut-point related to the atherogenic protein and the acute phase reactant and a fifth cut-point related to the anti-atherogenic protein,

20 (iv) a sixth cut-point related to the atherogenic protein and a seventh cut-point related to the acute phase reactant and the anti-atherogenic protein,

(v) an eighth cut-point related to the atherogenic protein and the anti-atherogenic protein and a ninth cut-point related to the acute phase reactant,

25 (vi) a tenth cut-point related to the atherogenic protein, the acute phase reactant, and the anti-atherogenic protein, and

(vii) an eleventh cut-point related to the atherogenic protein, a twelfth cut-point related to the acute phase reactant, and a thirteenth cut-point related to the anti-atherogenic protein;

(c) providing to the medical professional at least one of:

(i) a first value related to the level of the atherogenic protein and a second value related to the level of the acute phase reactant,

(ii) a third value related to the levels of the atherogenic protein and acute phase reactant,

(iii) a fourth value related to the levels of the atherogenic protein and acute phase reactant and a fifth value related to the level of the anti-atherogenic protein,

(iv) a sixth value related to the level of the atherogenic protein and a seventh value related to the levels of the acute phase reactant and anti-atherogenic protein,

(v) an eighth value related to the levels of the atherogenic protein and anti-atherogenic protein and a ninth value related to the level of the acute phase reactant, and

(vi) a tenth value related to the levels of the atherogenic protein, acute phase reactant, and anti-atherogenic protein,

(vii) an eleventh value related to the level of the atherogenic protein, a twelfth value related to the level of the acute phase reactant, and a thirteenth value related to the level of the anti-atherogenic protein; and

(d) providing to the medical professional the appropriate one or more of the cut-points to permit the medical professional to assess whether the patient is likely to have asymptomatic coronary artery disease based on at least one of the following:

(i) a comparison to the first cut-point of the first value and a comparison to the second cut-point of the second value,

(ii) a comparison to the third cut-point of the third value,

(iii) a comparison to the fourth cut-point of the fourth value and a comparison to the fifth cut-point of the fifth value,

(iv) a comparison to the sixth cut-point of the sixth value and a comparison to the seventh cut-point of the seventh value,

(v) a comparison to the eighth cut-point of the eighth value and a comparison to the ninth cut-point of the ninth value,

(vi) a comparison to the tenth cut-point of the tenth value, and

(vii) a comparison to the eleventh cut-point of the eleventh value, a comparison to the twelfth cut-point of the twelfth value, and a comparison to the thirteenth cut-point of the thirteenth value.

23. The method of claim 22 wherein the atherogenic protein comprises OxLDL.

24. The method of claim 23 wherein the OxLDL contains at least 60 substituted lysine residues per apo B-100 moiety.

25. The method of claim 22 wherein the acute phase reactant comprises a positive acute phase reactant or a negative acute phase reactant.

26. The method of claim 25 wherein the positive acute phase reactant is selected from the group consisting of C-reactive protein, serum amyloid A, von Willebrand factor, ferritin, and fibrinogen and the negative acute phase reactant is selected from the group consisting of albumin, apo A-I, apo A-II, and HDL.

27. The method of claim 22 wherein the anti-atherogenic protein comprises HDL.

28. The method of claim 22 wherein the atherogenic protein comprises OxLDL and the acute phase reactant is selected from the group consisting of C-reactive protein and fibrinogen.

29. The method of claim 28 wherein the anti-atherogenic protein is HDL.

30. The method of claim 22 wherein step (a) uses an immunological assay to obtain the level of atherogenic protein.

31. The method of claim 30 wherein the immunological assay uses one or more monoclonal antibodies each having an affinity for the atherogenic protein of at least about $5 \times 10^8 \text{ M}^{-1}$.

32. The method of claim 30 wherein the immunological assay uses at least one of the following monoclonal antibodies to obtain the level of atherogenic protein: mAb-4E6 produced by hybridoma Hyb4E6 deposited with the BCCM under deposit accession number LMBP 1660 CB, mAb-1H11 produced by hybridoma Hyb1H11 deposited with the BCCM under deposit accession number LMBP 1659 CB, and mAb-8A2 produced by hybridoma Hyb8A2 deposited with the BCCM under deposit accession number LMBP 1661 CB.

33. The method of claim 22 wherein the atherogenic protein comprises an atherogenic low density lipoprotein and step (a) is conducted using an immunological assay.

34. The method of claim 22 wherein the atherogenic protein comprises OxLDL and an immunological assay is used to obtain the level of atherogenic protein.

35. The method of claim 34 wherein the immunological assay uses one or more monoclonal antibodies each having an affinity for the atherogenic protein of at least about $5 \times 10^8 \text{ M}^{-1}$.
36. The method of claim 34 wherein in step (a) the level of anti-atherogenic protein is obtained and the anti-atherogenic protein comprises HDL.
- 5 37. The method of claim 34 wherein the acute phase reactant is selected from the group consisting of C-reactive protein and fibrinogen.
38. The method of claim 37 wherein in step (a) the level of anti-atherogenic protein is obtained and the anti-atherogenic protein comprises HDL.
39. The method of claim 34 wherein the OxLDL contains at least 60 substituted lysine
10 residues per apo B-100 moiety.
40. The method of claim 39 wherein in step (a) the level of anti-atherogenic protein is obtained and the anti-atherogenic protein comprises HDL.
41. The method of claim 40 wherein the acute phase reactant is selected from the group consisting of C-reactive protein and fibrinogen.
- 15 42. The method of claim 33 wherein the immunological assay uses at least one of the following monoclonal antibodies to obtain the level of atherogenic protein: mAb-4E6 produced by hybridoma Hyb4E6 deposited with the BCCM under deposit accession number LMBP 1660 CB, mAb-1H11 produced by hybridoma Hyb1H11 deposited with the BCCM under deposit accession number LMBP 1659 CB, and mAb-8A2 produced by hybridoma Hyb8A2 deposited
20 with the BCCM under deposit accession number LMBP 1661 CB.